

Polymer Translocation Through a Long Nanopore

Elena Slonkina

Department of Chemistry, Moscow State University, Moscow, Russia 119899

Anatoly B. Kolomeisky

Department of Chemistry, Rice University, Houston, TX 77005

Polymer translocation through a nanopore in a membrane investigated theoretically. Recent experiments on voltage-driven DNA and RNA translocations through a nanopore indicate that the size and geometry of the pore are important factors in polymer dynamics. A theoretical approach is presented which explicitly takes into account the effect of the nanopore length and diameter for polymer motion across the membrane. It is shown that the length of the pore is crucial for polymer translocation dynamics. The present model predicts that for realistic conditions (long nanopores and large external fields) there are two regimes of translocation depending on polymer size: for polymer chains larger than the pore length, the velocity of translocation is nearly constant, while for polymer chains smaller than the pore length the velocity increases with decreasing polymer size. These results agree with experimental data.

I. INTRODUCTION

Translocation of polymers across a nanopore plays a critical role in numerous natural phenomena and industrial processes. Many biological phenomena, such as the motion of DNA and RNA molecules across nuclear pores, virus infection of cells, DNA packaging into viral capsids, gene swapping and protein transport through membrane channels, involve the motion of biopolymers across membranes.^{1,2} In chemistry, the forced permeation of polymer molecules and electrophoresis are crucial for separations and purifications of synthetic as well as biological macromolecules. The motion of polymers in a confined medium is also technologically important in food and medicine production, in oil recovery and separation, and in many other industrial processes. Accordingly, the mechanisms of polymer translocation have become a subject of numerous experimental^{3,4,5,6,7,8,9} and theoretical studies.^{10,11,12,13,14,15,16,17}

A polymer molecule moving across a nanopore faces a large entropic barrier due to the decrease in the number of available configurations for polymer segments. In order to overcome this barrier and to speed up the motion of polymers, an external field or interaction is needed. In recent *in vitro* experiments,^{3,4,5,6,7,8,9} DNA and RNA molecules are driven through an α -hemolysin membrane channel with the help of an external electric field. These elegant experiments are based on the following simple idea. When a polymer molecule moves through a nanopore, the electric current in the system nearly vanishes because the polymer blocks the flow of free ions through the channel. Accurate recordings of current blockages allow the description of the dynamics of translocation of *single* polymer molecules. The principal experimental findings can be summarized as follows: (i) the ability of polymers to enter the nanopore depends linearly on polymer concentration and exponentially on applied voltage;^{3,6} (ii) there is a critical value of the external electric potential below which no polymer molecule can enter and move through the nanopore;^{6,7} (iii) the effective number of free charges on a translocating polymer is surprisingly very small in comparison with the number of available charges;⁶ (iv) there are two regimes of polymer threading through the nanopore depending on polymer length - long polymers move across the membrane with nearly constant velocity, while short polymers move significantly faster;⁷ (v) the nanopore length defines the boundary between short and long polymers.⁷ These last two experimental observations are the subject of the present theoretical investigations.

Several theoretical models^{10,11,12,13,14,15,16,17} have been developed in order to explain these experimental findings, however, with limited success. Theoretical approaches to polymer translocation mainly follows three directions. In one approach,^{10,14,17} the moving polymer molecule should overcome the entropic barrier, and the free energies of polymer segments determine the dynamics of translocation. Another approach¹³ focuses on the interaction between the polymer and the nanopore, and neglects the entropic contributions from polymer segments outside the nanopore. The last approach¹⁶ views the polymer translocation as the motion of a kink, which travels in the direction opposite to polymer transport. All these theoretical works provide a reasonable description of polymer threading through the nanopore for very large polymers. However, these theories are less successful in understanding the dynamics of relatively short polymers due to the fact that they view the nanopore as an object which can hold only one monomer (with the exception of Ref.¹⁷, as discussed below). The α -hemolysin membrane channel, that has been used as the nanopore in *in vitro* experiments,^{3,4,5,6,7,8,9} has a length of approximately 5 nm for the narrow part of the channel and thus can hold up to 10-15 DNA or RNA monomers. The theoretical approach of Ambjörnsson et al.¹⁷ takes into account the nanopore length and studies both the polymer entrance into the pore and the translocation process. However, only ideal flexible polymers are considered and theoretical analysis focused on the dependence of polymer translocation dynamics on external electric field.

In this work the effects of the nanopore length and diameter on the threading dynamics of single polymer molecules are investigated. The goal is to develop the simplest theoretical description of translocation process which takes into account the geometry of the nanopore and interactions between the nanopore and polymer molecule. In the present model the polymer moves across the membrane as shown in Fig.1. The article is organized as follows. In Section II we develop a model and calculate free energies and translocation times for translocating polymers of different sizes. In Section III we apply our results for the description of experimental translocations of voltage-driven DNA molecules. Our theoretical analysis is summarized in Section IV.

II. MODEL FOR POLYMER TRANSLOCATION

Consider a polymer molecule consisting of N monomers (each of size a), which moves from an upper chamber to a lower chamber through a nanopore of length $l = Ma$ and diameter $d = Da$, as shown in Fig.1. Here we assume that as soon as the polymer enters into the pore, it is unlikely to come back. This assumption is justified since under experimental conditions the energy gained by a single monomer by moving through the nanopore is much larger than the thermal energy, and thus the probability to return is very small.¹⁷ It is also assumed that the nanopore is part of an infinite two-dimensional membrane, and there are no interactions between the polymer and the membrane. Let the chemical potential of the monomer in the upper region, in the nanopore, and in the lower region be μ_1 , μ_2 and μ_3 respectively (see Fig.1). The potential energy change is considered to occur only across the nanopore.

The simple visual analysis of polymer transport across the nanopore indicates that the motion of long polymers (larger than the nanopore length) is qualitatively different from that of short polymers, and these two cases must be considered separately. In our analysis, we assume that both N and M are large, which is consistent with current experimental conditions.^{3,4,5,6,7,8,9} In our theoretical model the translocation process starts as soon as the first monomer enters the pore, and ends when the last monomer leaves the pore. Note that experimental translocation times are slightly different, as discussed below.

A. Polymers with sizes $N > M$

In this case, there are three regimes of motion, as shown in Fig.2a. In regime I, the leading monomer enters the nanopore from the upper region and then moves across the nanopore. In regime II, the leading monomer leaves the nanopore, while the end monomer approaches the entrance of the pore. In regime III, the end monomer goes through the nanopore and finally leaves it for the lower region. Assuming that the polymer segments inside the nanopore do not contribute to the free energy, i.e., there are no fluctuations inside the pore, the free energy F_m of the polymer configuration in regime I with m monomers in the pore and $(N - m)$ monomers in the upper region, is given by¹⁴

$$\frac{F_m}{k_B T} = (1 - \gamma'_1) \ln(N - m) + \frac{m \Delta \mu_1}{k_B T}, \quad (1)$$

where γ'_1 is a parameter which describes the properties of polymers and which is equal to 0.5, 0.69 and 1 for Gaussian, self-avoiding, and rod-like chains, respectively;¹⁸ the subindex 1 indicates the properties of the upper region of the system. The first term in (1) is an entropic contribution due to $(N - m)$ free monomers in the upper region, while the second term represents the energy gain due to moving m monomers into the pore, and includes the effect of the external field and chemical potential changes. The entropic contribution term follows from the partition function for the polymer chain in a semi-infinite space near a hard wall with the end monomer anchored at the wall.^{14,18} The chemical potential difference per monomer is given by $\Delta\mu_1 = \mu_2 - \mu_1$, and we assume that the potential energy inside the nanopore is uniform. Note that the number of monomers in the pore m can vary between 0 and M . Similarly, the translocation of the polymer in regimes II and III can be described by

$$\frac{F_m}{k_B T} = (1 - \gamma'_1) \ln(N - M - m) + (1 - \gamma'_2) \ln m + \frac{m\Delta\mu_3}{k_B T}, \quad (2)$$

with $0 < m < N - M$, and

$$\frac{F_m}{k_B T} = (1 - \gamma'_2) \ln m + \frac{m\Delta\mu_2}{k_B T}, \quad (3)$$

with $N - M < m < N$, respectively. Here γ'_2 describes the properties of the polymers in the lower region, and the chemical potential differences are $\Delta\mu_2 = \mu_3 - \mu_2$ and $\Delta\mu_3 = \mu_2 - \mu_1 + \mu_3 - \mu_2 = \Delta\mu_1 + \Delta\mu_2$.

The transport of the polymer across the nanopore can be described by a Master equation¹⁴

$$\frac{\partial P_m(i, t)}{\partial t} = u_{m-1} P_{m-1}(i, t) + w_{m+1} P_{m+1}(i, t) - (u_m + w_m) P_m(i, t), \quad (4)$$

where $P_m(i, t)$ is the probability of moving m monomers in regime $i = \text{I, II or III}$ at time t . u_m is the rate constant of adding one more monomer to the segment of m monomers already moved, and w_m is the rate constant of removing one monomer from the segment of length m . These rate constants are related by detailed balance, namely,

$$\ln \frac{u_m}{w_{m+1}} = -\frac{(F_{m+1} - F_m)}{k_B T}. \quad (5)$$

Following Muthukumar,¹⁴ it is assumed that these rate constants are independent of m ; however, they are different for different regimes, i.e., $u_m = u_i$ for $i = \text{I, II or III}$, and generally $u_1 \neq u_2 \neq u_3$. Transforming the discrete Eq. (4) into continuum Smoluchovskii

equation, we obtain

$$\frac{\partial P_m(i, t)}{\partial t} = \frac{\partial}{\partial m} \left[\frac{u_i}{k_B T} \frac{\partial F_m}{\partial m} P_m(i, t) + u_i \frac{\partial}{\partial m} P_m(i, t) \right]. \quad (6)$$

The mean translocation time τ can now be calculated as a sum of mean first-passage times in each regime,¹⁹ i.e., $\tau = \tau_1 + \tau_2 + \tau_3$, with

$$\tau_1 = \frac{1}{u_1} \int_0^M \exp\left(\frac{F_{m_1}}{k_B T}\right) dm_1 \int_0^{m_1} \exp\left(-\frac{F_{m_2}}{k_B T}\right) dm_2, \quad (7)$$

$$\tau_2 = \frac{1}{u_2} \int_0^{N-M} \exp\left(\frac{F_{m_1}}{k_B T}\right) dm_1 \int_0^{m_1} \exp\left(-\frac{F_{m_2}}{k_B T}\right) dm_2, \quad (8)$$

$$\tau_3 = \frac{1}{u_1} \int_{N-M}^N \exp\left(\frac{F_{m_1}}{k_B T}\right) dm_1 \int_0^{m_1} \exp\left(-\frac{F_{m_2}}{k_B T}\right) dm_2, \quad (9)$$

where the corresponding expressions for free energies in different regimes are used. These equations can be solved numerically for any set of parameters; however, explicit analytic results can be obtained in some special cases. Chemical potential differences are the leading factors in the dynamics of translocation.^{14,15} Then, for $\Delta\mu_1 = \Delta\mu_2 = \Delta\mu_3 = 0$, we can obtain exact expressions for translocation times; namely, τ_i are given by

$$\tau_1 = \frac{N^2}{u_1 \gamma'_1} \left[\frac{1 - (1 - M/N)^{2-\gamma'_1}}{2 - \gamma'_1} - \frac{1 - (1 - M/N)^2}{2} \right], \quad (10)$$

$$\tau_2 = \alpha \frac{(N - M)^2}{u_2}, \quad (11)$$

$$\tau_3 = \frac{N^2}{u_3(2 - \gamma'_2)} \left[\frac{1 - (1 - M/N)^{\gamma'_2}}{\gamma'_2} - \frac{1 - (1 - M/N)^2}{2} \right], \quad (12)$$

where α is a constant, which is equal to $1/2$ and $\pi^2/16$ for the special cases $\gamma'_1 = \gamma'_2 = 1$ and $\gamma'_1 = \gamma'_2 = 1/2$, respectively. In the limit $N \gg M$, these results reduce to

$$\tau_1 \simeq \frac{M^2}{2u_1}, \quad \tau_2 \simeq \frac{\alpha N^2}{u_2}, \quad \tau_3 \simeq \frac{M^2}{2u_3}. \quad (13)$$

Thus the overall translocation time τ in this limit is proportional to N^2 , in agreement with the corresponding results from Ref.¹⁴. For another limiting case, $N \sim M$, we obtain in a similar way

$$\tau_1 \simeq \frac{N^2}{2u_1(2 - \gamma'_1)}, \quad \tau_2 \simeq 0, \quad \tau_3 \simeq \frac{N^2}{2u_3\gamma'_2}. \quad (14)$$

In this case, the overall translocation time is also proportional to N^2 , however, with a different coefficient.

For more realistic situations, when the chemical potential differences are negative and the entropic terms in Eqs.(1,2,3) are weak in comparison with the $\Delta\mu_i$ terms, we obtain in regime I

$$\tau_1 \simeq \begin{cases} \frac{k_B T M}{u_1 |\Delta\mu_1|}, & M|\Delta\mu_1| > 1, \\ \frac{M^2}{2u_1}, & M|\Delta\mu_1| < 1, \end{cases} \quad (15)$$

in regime II,

$$\tau_2 \simeq \begin{cases} \frac{k_B T (N-M)}{u_2 |\Delta\mu_3|}, & (N-M)|\Delta\mu_3| > 1, \\ \frac{(N-M)^2}{2u_2}, & (N-M)|\Delta\mu_3| < 1, \end{cases} \quad (16)$$

and in regime III,

$$\tau_3 \simeq \begin{cases} \frac{k_B T M}{u_3 |\Delta\mu_2|}, & M|\Delta\mu_2| > 1, \\ \frac{M^2}{2u_3}, & M|\Delta\mu_2| < 1. \end{cases} \quad (17)$$

For large positive chemical potential differences we can easily calculate for different regimes

$$\tau_1 \simeq \frac{1}{u_1} \left(\frac{k_B T}{u_1 \Delta\mu_1} \right)^2 \exp \left(M \frac{\Delta\mu_1}{k_B T} \right), \quad (18)$$

$$\tau_2 \simeq \frac{1}{u_2} \left(\frac{k_B T}{u_2 \Delta\mu_3} \right)^2 \exp \left((N-M) \frac{\Delta\mu_3}{k_B T} \right), \quad (19)$$

$$\tau_3 \simeq \frac{1}{u_3} \left(\frac{k_B T}{u_3 \Delta\mu_2} \right)^2 \exp \left(M \frac{\Delta\mu_2}{k_B T} \right). \quad (20)$$

When $N \gg M$, the translocation time τ is governed by the dynamics in regime II, and it becomes proportional to the polymer length for large negative chemical potential differences, in agreement with experimental observations.^{3,7}

B. Polymers with sizes $N < M$

For relatively short polymers (but recall that $N \gg 1$), again three regimes of translocation are observed, as shown in Fig. 2. The motion in regimes I and III is qualitatively similar to the transport of long polymers (compare Fig.2a and Fig.2b); however the transport in regime II is *different*, since there are no polymer segments in the upper or lower regions. Thus the free energy expressions in regimes I and III are the same as those given by Eqs.

(1) and (3), respectively with, however, $0 < m < N$ in both regimes. The free energy in regime II can be taken equal to zero because at this level of approximation we neglect the free energy contribution from the polymer segments fluctuating inside the nanopore.

Calculations of translocation times can be performed in a similar fashion as was done for long polymers. First, for translocation time in regime II at all possible values of parameters, it can be easily computed,

$$\tau_2 = \frac{(N - M)^2}{2u'_2}, \quad (21)$$

where it is assumed that $u'_2 \neq u_2$ because the translocation process is physically different in this regime for short polymers in comparison with long polymers.

When $\Delta\mu_1 = \Delta\mu_2 = 0$, the translocation times in regimes I and III are equal to

$$\tau_1 = \frac{N^2}{2u_1(2 - \gamma'_1)}, \quad \tau_3 = \frac{N^2}{2u_3\gamma'_2}. \quad (22)$$

Here we assume that the rate constants for long and for short polymers are the same, since the dynamics of translocation in these regimes are very similar for short and for long polymers. For more realistic situations, when $\Delta\mu_1 < 0$ and $\Delta\mu_2 < 0$, and the entropic terms in the free energy expressions are small, the calculations in regime I yield

$$\tau_1 \simeq \begin{cases} \frac{k_B T N}{u_1 |\Delta\mu_1|}, & N|\Delta\mu_1| > 1, \\ \frac{N^2}{2u_1}, & N|\Delta\mu_1| < 1, \end{cases} \quad (23)$$

and in regime III

$$\tau_3 \simeq \begin{cases} \frac{k_B T N}{u_3 |\Delta\mu_2|}, & N|\Delta\mu_2| > 1, \\ \frac{N^2}{2u_3}, & N|\Delta\mu_2| < 1. \end{cases} \quad (24)$$

For large positive chemical potential differences, translocation times are given by

$$\tau_1 \simeq \frac{1}{u_1} \left(\frac{k_B T}{u_1 \Delta\mu_1} \right)^2 \exp \left(N \frac{\Delta\mu_1}{k_B T} \right), \quad (25)$$

$$\tau_3 \simeq \frac{1}{u_3} \left(\frac{k_B T}{u_3 \Delta\mu_2} \right)^2 \exp \left(N \frac{\Delta\mu_2}{k_B T} \right). \quad (26)$$

C. Fluctuations inside the nanopore

So far in our calculations of polymer translocation times we neglected the contributions from the fluctuations of polymer segments inside the nanopore, although these fluctuations

may be important. To take them into account the scaling analysis can be used to describe the polymer molecule inside the confined cylindrical pore.²⁰ The free energy of confined polymer chain is given by $k_B T N_b$, where $N_b = l/d$ is the number of blobs inside the pore.²⁰ Note, however, that this approach is valid when $d \ll l$. The size of each blob is equal to the diameter of the pore, i.e.,

$$d = Da = ag^\nu, \quad (27)$$

where g is the number of monomers in the blob, and the exponent ν is equal to $1/2$, $3/5$, and 1 for ideal, self-avoiding, and rod-like chains, respectively. Then the maximum number of monomers in the pore of length $l = Ma$ and diameter $d = Da$ is given by

$$M_{max} = \frac{l}{d}g = MD^{(1/\nu-1)}. \quad (28)$$

Note that for rod-like chains $M_{max} = M$, while for ideal flexible chains $M_{max} = MD$.

Knowing the free energy contribution of polymer segments inside the nanopore allows to calculate the translocation dynamics as discussed in detail above. Consider first the dynamics of the polymer molecule in regime II. The contribution from the fluctuating polymer segments inside the pore is always constant in this regime because the number of monomers inside the nanopore does not change. Then this free energy term will not affect translocation times since they are determined by free energy differences [see Eqs.(15),(16),(17)]. In regimes I and III the number of monomers inside the nanopore is changing, however the free energy difference from this confinement term is equal to $k_B T D^{-1/\nu}$, which for experimental conditions^{3,5,6} is very small in comparison with entropic and chemical potential terms, and can be neglected. Thus the free energy contributions from fluctuating monomers inside the nanopore do not change the results on translocation dynamics of the polymers (provided that M is replaced by M_{max}).

III. COMPARISON WITH EXPERIMENTS

The above results are well compared with the experimental findings of Ref.⁷, where the size dependence of voltage-driven single-stranded DNA molecules has been investigated. In the present theoretical approach, the process of translocation is assumed to start as soon as the leading monomer enters the nanopore and to end when the end monomer leaves the

nanopore. Then the translocation velocity is given by

$$V = (N + M)a/\tau. \quad (29)$$

For realistic situations (large N and M , $\Delta\mu_i \ll 0$), the results for translocation times in corresponding regimes [see Eqs. (15),(16),(17),(21) and (22)] can be substituted into equation (29), leading to explicit expressions for the translocation velocity

$$V = \begin{cases} (N + M)a / \left(\frac{k_B T M}{u_1 |\Delta\mu_1|} + \frac{k_B T (N-M)}{u_2 |\Delta\mu_3|} + \frac{k_B T M}{u_3 |\Delta\mu_2|} \right), & N > M, \\ (N + M)a / \left(\frac{k_B T N}{u_1 |\Delta\mu_1|} + \frac{(M-N)^2}{2u'_2} + \frac{k_B T N}{u_3 |\Delta\mu_2|} \right), & N < M. \end{cases} \quad (30)$$

However, in the experiments of Meller et al.,⁷ the translocation time was measured only when a current passing through the nanopore dropped to a level below 65% of an open channel current. The authors also showed that the blockade level is proportional to the fractional volume of the channel occupied by the polymer. This means that in these experiments the translocation process started when 35% of the polymer entered into the nanopore, and ended when only 35% of the polymer left in the pore. Thus, in order to compare our theoretical predictions with experimental observations, the expressions for translocation velocity (30) should be modified as follows

$$V = \begin{cases} (N + 0.30M)a / \left(\frac{0.65Mk_B T}{u_1 |\Delta\mu_1|} + \frac{k_B T (N-M)}{u_2 |\Delta\mu_3|} + \frac{0.65Mk_B T}{u_3 |\Delta\mu_2|} \right), & N > M, \\ (N + 0.30M)a / \left(\frac{k_B T (N-0.35M)}{u_1 |\Delta\mu_1|} + \frac{(M-N)^2}{2u'_2} + \frac{k_B T (N-0.35M)}{u_3 |\Delta\mu_2|} \right), & N < M. \end{cases} \quad (31)$$

Under experimental conditions,⁷ the single-stranded DNA molecules behave more like rod-like polymers, and this fact justifies using $M_{max} = M$ in our description of experimental data. Then the expressions (31) can be used to fit the observed translocation velocities⁷ as shown in Fig.3. The present theoretical approach predicts two types of translocation depending on polymer size. For large polymers, larger than the nanopore length, the translocation velocity approaches a constant value, while for short polymers the velocity increases significantly with decreasing polymer length. These predictions are in excellent qualitative and quantitative agreement with experiments for large polymers; however, for short polymers the agreement is only qualitative.

There are several reasons to explain the deviations between the presented theory and experimental behavior for short polymers. In our theoretical approach we used a polymer description of molecule dynamics, while for such short polynucleotides ($N = 4-12$)

the polymer description is probably less precise and the discrete chemical nature of the molecules should be taken into account. In addition, our descriptions of the nanopore geometry and the potential changes inside the nanopore are very simplified. However, for short polymer molecules these factors probably influence the translocation dynamics much stronger than for large polymers. Despite these discrepancies, the fact that a very simple theoretical approach can provide a qualitative and semi-quantitative description of complex translocation processes is rather encouraging. It also indicates that the presented theoretical model correctly captures and describes the main features of translocation phenomena.

Our theoretical approach allows us to investigate the effect of interactions between the nanopore and the polymer molecule. The rate constants u_j measure the degree of such interactions. The smaller the rate constants, the larger the attraction between the moving polymer chains and the nanopore. As shown in Fig.4, when only the rate constants for short polymers in regime II are varied, the interactions between the nanopore and the polymer can change the translocation dynamics significantly. The stronger the interaction, the slower the motion of threading polymer molecules, in agreement with intuition.

IV. SUMMARY AND CONCLUSIONS

A simple theoretical model of polymer translocation through the long nanopores driven by external electric fields is presented. The fact that we take into account the nanopore length and diameter allows us to describe the translocation dynamics for polymer molecules of different sizes. By considering in detail different regimes of moving polymers across the membranes, the general expressions for free energies and translocation times for polymer chains threading through the nanopores are derived. The presented theoretical predictions are compared with experimental results on voltage-driven translocations of single-stranded DNA molecules through the α -hemolysin protein channels.⁷ It is found that for experimental conditions,⁷ long polymers, longer than the nanopore length, translocate with nearly constant velocity, while short polymers move significantly faster. The theoretical analysis indicates that for experiments⁷ with α -hemolysin protein channels the polymer fluctuations inside the nanopore do not affect the translocation dynamics. Presented theoretical results are in agreement with experimental observations.

Although a reasonable description of polymer translocation experiments⁷ is provided,

there are many factors that have not been taking into account. We assumed in our calculations that the external field inside the nanopore is uniform, while more realistic picture would incorporate a potential profile inside the nanopore,¹⁷ which can be found by taking into account the realistic geometry of the nanopore and all electrostatic interactions. In the present model, the possibility that the polymer molecule can return was neglected, which is a very good approximation at large external driving fields, as realized in most experiments. Given theoretical approach allows to consider this effect by solving the Smoluchovskii equations (6) with different boundary conditions. We also assumed that the nanopore is very narrow, i.e., the effect of the nanopore diameter on free energies of the polymer segments outside of the pore has not been considered, although the α -hemolysin pore in principle can hold several monomers of DNA or RNA molecules. Probably, the simplest way to include this possibility into presented theoretical model, is to utilize the scaling approach.²⁰

Acknowledgments

ABK is grateful to Dr. A. Meller for introducing to this problem and for valuable discussions. The critical comments by Profs. M. Robert, M.E. Fisher, and M. Pasquali, Dr. P. Willis and A. Montesi are highly appreciated. The financial support of the Camille and Henry Dreyfus New Faculty Awards Program (under Grant NF-00-056) is gratefully acknowledged. The authors are also grateful to Center of Biological and Environmental Nanotechnology at Rice University for financial support.

¹ H. Lodish, *et al.*, *Molecular Cell Biology*, 3rd Edition (Scientific American Books, New York, 1995).

² B. Alberts, *et al.*, *Molecular Biology of the Cell*, 3rd Edition (Garland Publishing, New York, 1994).

³ J. J. Kasianowich, E. Brandin, D. Branton, and D. W. Deamer, *Proc. Natl. Acad. Sci. USA* **93**, 13770 (1996).

⁴ M. Akeson, D. Branton, J. J. Kasianowich, E. Brandin, and D. W. Deamer, *Biophys. J.* **77**, 3227 (1999).

- ⁵ A. Meller, L. Nivon, E Brandin, J. Golovchenko, and D. Branton, Proc. Natl. Acad. Sci. USA **97**, 1079 (2000).
- ⁶ S. E. Henrickson, M. Misakian, B. Robertson, and J. J. Kasianowich, Phys. Rev. Lett. **85**, 3057 (2000).
- ⁷ A. Meller, L. Nivon, and D. Branton, Phys. Rev. Lett. **86**, 3435 (2001).
- ⁸ L. Movileanu and H. Bayley, Proc. Natl. Acad. Sci. USA **98**, 10137 (2001).
- ⁹ S. Howorka, L. Movileanu, O. Braha and H. Bayley, Proc. Natl. Acad. Sci. USA **98**, 12996 (2001).
- ¹⁰ W. Sung and P.J. Park, Phys. Rev. Lett. **77**, 783 (1996).
- ¹¹ E. A. Di Marzio and A. J. Mandell, J. Chem. Phys. **107**, 5510 (1997).
- ¹² P.-G. de Gennes, Adv. Polym. Sci. **138**, 91 (1999).
- ¹³ D. K. Lubensky and D. R. Nelson, Biophys. J. **77**, 1824 (1999).
- ¹⁴ M. Muthukumar, J. Chem. Phys. **111**, 10371 (1999).
- ¹⁵ M. Muthukumar, Phys. Rev. Lett. **86**, 3188 (2001).
- ¹⁶ K.L. Sebastian and A.K.R. Paul, Phys. Rev. E **62**, 927 (2000).
- ¹⁷ T. Ambjörnsson, S.P. Apell, Z. Konkoli, E.A. Di Marzio and J.J. Kasianowicz, J. Chem. Phys. **117**, 4063 (2002).
- ¹⁸ E. Eisenriegler, *Polymers Near Surfaces* (World Scientific, Singapore, 1993).
- ¹⁹ H. Risken, *The Fokker-Planck Equation* (Springer-Verlag, Berlin, 1989).
- ²⁰ P.-G. de Gennes, *Scaling Concepts in Polymer Physics* (Cornell University Press, 1979).

Figure Captions

Fig. 1. A polymer molecule moves from the upper chamber to lower through a cylindrical nanopore of length l and diameter d . The potential energy change is considered to be only inside the nanopore. In polymer translocation experiments (see Refs.^{3,4,5,6,7,8,9}), $l \simeq 5$ nm, $d \simeq 2$ nm, and $\Delta V \simeq 50\text{--}300$ mV.

Fig. 2. Three regimes of translocation for polymers of different sizes: a) for long polymers, b) for short polymers. The size of the nanopore is $l = Ma$. Solid filled circles indicate the head and the end monomer of the polymer molecule.

Fig. 3. Translocation velocity as a function of polymer size. The length of a nanopore is equal to $12a$, where the monomer size is given by $a = 4 \times 10^{-4}$ μm . Filled squares are experimental observations from Ref.⁷ obtained at external field of 120 mV. Solid lines are our fits with $\Delta\mu_1 = \Delta\mu_2 = 2.5k_B T$, $u_1 = u_3 = 2.3 \times 10^4$ s^{-1} , $u_2 = 1.4 \times 10^4$ s^{-1} , and $u'_2 = 4.5 \times 10^6$ s^{-1} . Eq. (31) is used to calculate theoretical curves.

Fig. 4. Translocation velocities for different degrees of interactions between the nanopore and the polymers. Solid curve is the same as in Fig.3 with $u'_2 = 4.5 \times 10^6$, while dashed curve is for the case when $u'_2 = 1.0 \times 10^6$, dot-dashed curve is for the case when $u'_2 = 0.5 \times 10^6$, and dotted curve is for the case when $u'_2 = 0.2 \times 10^6$.

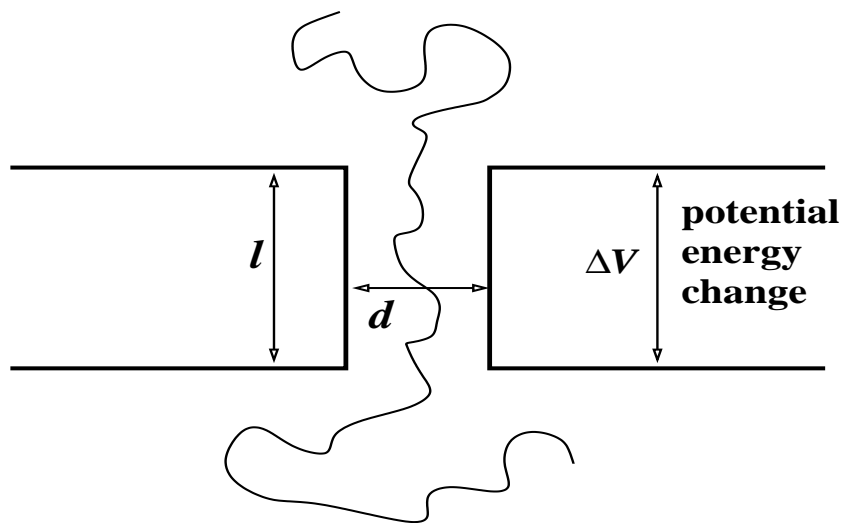


Figure 1. Slonkina and Kolomeisky

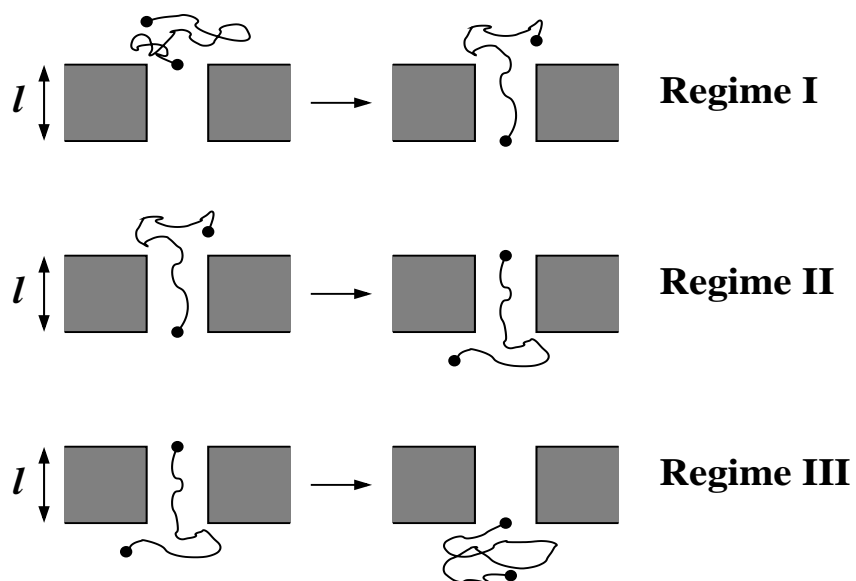


Figure 2a. Slonkina and Kolomeisky

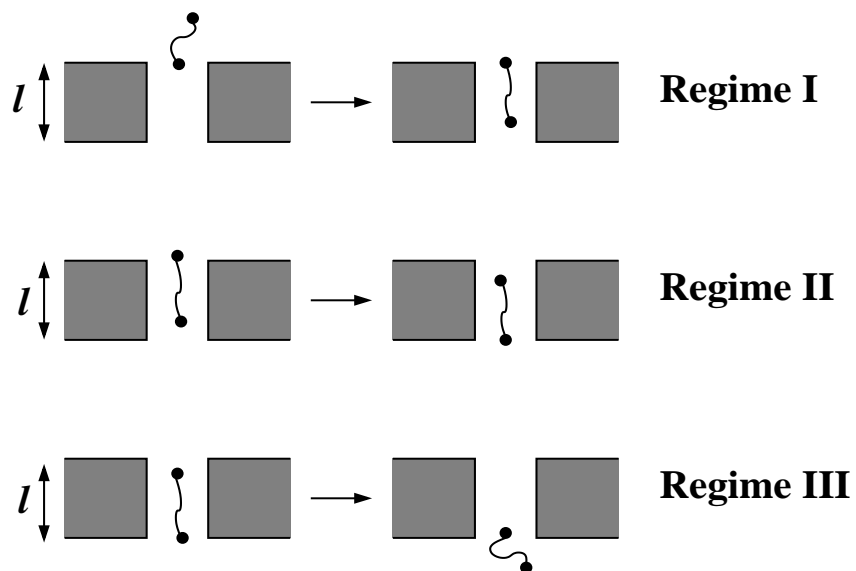


Figure 2b. Slonkina and Kolomeisky

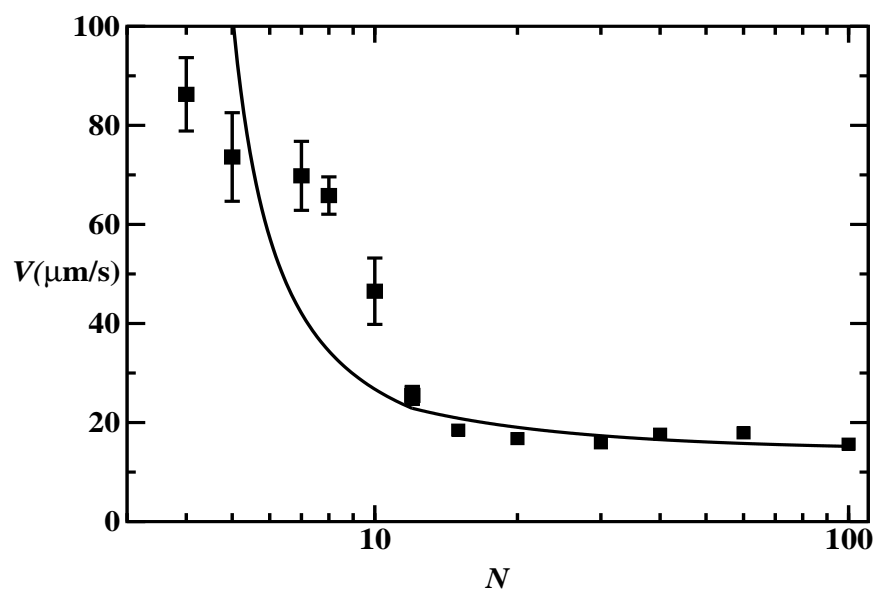
Figure 3. Slonkina and Kolomeisky

Figure 4. Slonkina and Kolomeisky